Orthopaedic and Rehabilitation Devices Panel
Of the Medical Devices Advisory Committee
November 21, 2002
Draft Questions

SPINE

In January of 2000, the FDA issued The Guidance Document for the Preparation of IDEs for spinal systems. Prior to its issuance, ORDB presented a preliminary background document to the Orthopedic and Rehabilitation Devices Panel. During the October 8, 1998 panel meeting, input was received from panel members and the public which resulted in the current guidance document. At that time, the FDA requested some input on Non-Fusion devices which are *not* intended to facilitate fusion of the spine. Unlike fusion devices, these devices allow some functional motion through the various levels of the spine. These include devices that provide stability while continuing to allow some percentage of normal or functional motion, devices which allow motion and growth, and devices which stabilize vertebral body and spine fracture repair. Examples of these types of devices are included in the references enclosed in this panel package.

The current spinal guidance focuses primarily on spinal fusion devices for various etiologies, with brief guidance on such non fusion devices as vertebral body replacements and disc replacement devices. While the FDA Guidance for Spinal Implant 510 (k)s issued September 27, 2000, outlines in detail devices intended for fusion and there is a voluntary testing standard available for pedicle screw systems and intervertebral body fusion devices (i.e., ASTM F1717 and ASTM 2077, respectively), many sponsors use modified versions to address different types of spinal systems. Because there are testing standards in development, the FDA has advised sponsors to contact appropriate standards bodies (e.g., ASTM, ISO) for additional information. As the scope of spinal devices expands, the FDA recognizes the need to update the spinal guidance to include additional clarification and suggestions for preclinical testing, clinical assessments, endpoints and success determinations related to emerging spinal technologies.

I. Preclinical Questions

1. Currently, the FDA Guidance for Spinal Implant 510(k)'s, which extensively covers devices intended for fusion, recommends various static and fatigue testing for spinal devices. Because devices not intended for fusion are intended to stabilize the spinal motion segment and retain functional motion, they must be designed to last for the lifetime of the individual rather than until a fusion occurs. Therefore, the current testing requested for devices intended for non-fusion may not be adequate. In addition, the current testing for fusion devices made of materials other than stainless steel and titanium may not be adequate. The FDA currently requests the following testing for spinal devices:

   Fusion devices (devices intended to stabilize by fusing motion segments, e.g., pedicle screw systems, intervertebral fusion devices, vertebral body fusion devices, etc.)

?? Fatigue - The fatigue testing should involve a minimum of six samples of the worst case construct to generate a stress (load) versus number of cycles (S/N) curve that characterizes the asymptotic endurance limit (e.g., a minimum of two samples per load level with one load level reaching a run out value of five million cycles) compared to a appropriate control device. Rationale for the components chosen as worst case should be provided. The interconnection mechanisms/systems may be tested in the same set of constructs or each in a separate set of constructs. Each interconnection mechanism should be tested or an adequate rationale for not testing an interconnection should be provided. Additionally, testing should be performed out to a minimum run out of 10 million cycles for intervertebral body replacement devices intended for tumor patients because these patients may present a great difficulty in achieving fusion, and, therefore, the device is acting more as a stabilizer.

?? Static - The testing should involve a minimum of five samples of the worst case construct. As with the fatigue testing, the components tested and the loading mode should be justified.

Examples of the types of construct testing typically performed for a given type of spinal system in order to establish relative safety are as follows:

? For lumbar and thoracic pedicle screw systems that are intended for fusion, static and fatigue bending testing should be provided (e.g., ASTM F1717).

? For cervical, pedicle or lateral mass systems intended for fusion, static and fatigue testing should be provided. The loading mode (torsional or bending) is dependent on the design and material.

? For intervertebral body fusion devices, static, fatigue, and expulsion (push-out testing) testing should be provided. The loading mode (axial, torsional, bending, and/or shear) is dependent on the design, material, and levels of use.

? For vertebral body replacement devices, static and fatigue testing in bending and torsional loading modes should be provided.

Non-Fusion devices (devices intended to stabilize yet retain functional motion, e.g., disc nucleus replacements, intervertebral disc prosthesis, screw or hook based stabilization spinal systems without attempting fusion)
These are some of the items FDA believes may be appropriate to consider:

? Compression Fatigue - The fatigue testing should involve a minimum of six samples of the worst case construct to generate a stress (load) versus number of cycles (S/N) curve that characterizes the asymptotic endurance limit (e.g., a minimum of two samples per load level with one load level reaching a run out

value of ten million cycles) compared to a appropriate control device. Rationale for the components chosen as worst case should be provided.

?? Durability Testing – The durability testing should involve cyclic loading testing several loading modes (e.g., flexion/extension, lateral bending, and axial rotation) and involve a minimum of six samples of the worst-case construct out to ten million cycles. This test can either be combined to incorporate all testing directions into one test, or separated into each loading mode. Durability testing establishes loading direction, stability of the device, and wear generation potential. Clinical justification for the loads and angles chosen should be provided.

? Static Compression - The testing should involve a minimum of five samples of the worst case construct. As with the fatigue testing, the components tested and the loading mode should be justified.

?? Other potential tests –

- ?? Migration/Expulsion testing
- ?? Static and Dynamic Shear Testing
- ?? Creep and Stress Relaxation Testing

Examples of the types of construct testing typically performed for a given type of spinal system in order to establish relative safety are as follows:

? For vertebral disc replacements, static and fatigue tests in multiple loading modes should be provided out to 10 million cycles.

?? For a stabilization pedicle screw system intended for non-fusion, dynamic shear testing and torsion testing should be provided.

?? For nucleus replacements, expulsion testing should be provided.

?? For nucleus replacements, fatigue compression tests on new and "aged" devices should be provided.

?? For devices with polymer components (e.g., polyethylene cords, poyletheretherketone components, etc) creep and/or stress relaxation testing should be provided.

Depending on the design of the system, the sponsor may need to perform different tests in lieu of those identified above, perform additional tests in different testing modes, provide testing on individual components of the subject system, etc.

While there is a voluntary testing standard available for pedicle screw systems intended for fusion and intervertebral body fusion devices (i.e., ASTM F1717 and

ASTM 2077, respectively), many sponsors use modified versions to address different types of spinal systems. Because there are testing standards in development, sponsors are advised to contact appropriate standards bodies (e.g., ASTM, ISO) for information regarding test set-ups, parameters, etc. for their specific device type.

- ?? Please comment on the currently recommended preclinical mechanical, debris, or wear testing to evaluate new materials, device properties/integrity and wear debris for fusion and non-fusion devices.
- ?? Discuss what additional testing, if any, should be added to current testing recommendations for the following devices
  - ?? Stabilization devices for non-fusion
  - ?? Intervertebral disc/joint replacements (cervical/thoracolumbar)
  - ?? Devices manufactured out of new materials.
  - ?? Intervertebral disc nucleus replacements

2. The FDA is currently requesting information for any device used in the area of the spinal cord and nerve roots, that has the potential to generate debris, regarding local and systemic adverse effects. For those incorporating new materials (e.g.., polymers, composites, etc.) or designs, both fusion and non fusion, the FDA recommends that manufacturers perform wear simulations and fatigue tests to evaluate the potential for the device to generate wear debris. The FDA believes the wear debris generated from these tests should be collected and characterized. For those devices where this may be an issue, the FDA suggests two options:

   - ?? Injection study of various sized particles into the spinal cord area of small animals
   - ?? Functional animal models

   Because of the limitations of the current testing methods and models, should devices made of new materials and/or those intended to retain motion be tested for local and systemic adverse effects independent of the type of material or the amount of wear debris generated? If you suggest that testing be performed, please describe the testing you recommend. For example,
   - ?? Discuss viability and usefulness of injection animal study including amount and distribution of sizes and shapes of wear debris should be injected in the animal in predicting what may occur clinically for the life of the implant;
   - ?? Discuss recommendations, viability and usefulness of functional animal models in predicting what may occur clinically for the life of the implant; or
   - ?? Discuss alternatives.

II. Clinical Questions

1. For spinal assemblies not intended to fuse motion segments (Non-fusion spinal devices, e.g., disc replacement devices, nucleus replacement devices, joint replacement, spinal stabilization without fusion, etc.), the goals of treatment may be

to stabilize the spine, maintain "normal/functional" motion, treat disease early in its course to prevent further progression and to conserve motion instead of fusing segments of the spine to alleviate pain and restore function. These types of devices provide challenges in choosing the best methods to evaluate safety and effectiveness.

Our current Spinal Guidance describes methods to assure that data collected provide adequate characterization of the safety and effectiveness of devices. These sections suggest appropriate patient inclusion and exclusion criteria (Section 4 and 5), effectiveness evaluations (Section 8: 8.1-8.4) safety evaluations (Section 9) and patient and study success criteria (Section 10). The FDA believes that the populations and goals of treatment may be different for devices that maintain functional motion. Therefore:

a. Please discuss study designs which may be better suited to evaluate Non-Fusion spinal devices. In your discussion, please comment on:
   i. enrollment criteria,
   ii. patient populations,
   iii. controls,
   iv. success criteria and
   v. goals of the study

   that would be suitable for these types of Non-fusion spinal devices.

b. Devices intended to stabilize the spine yet retain functional motion are expected to have an upper limit of motion beyond which one would consider the device to be unstable and a lower limit below which one would consider the device to have inadequate motion or possibly even consider the segment to be fused. Please discuss the amount of motion and on what scale, to define a patient as a functional and clinical success (i.e., a clinically significant improvement in condition) for each of cervical, thoracic and lumbar levels for Non-Fusion spinal devices.

III. Vertebroplasty (see enclosed references)

There is a growing body of literature describing devices to be used for the treatment of insufficiency fractures due to neoplasm or osteoporosis, either for stabilization or reduction of the fracture. These devices include high and low modulus bone cements and other non-resorbable and absorbable bone cement alternatives. As with other devices, these devices and procedures are emerging as new technologies for treating fractures in the spine, and the FDA considers these devices as permanent implants in the spine.

1. Describe the current treatment alternatives for the treatment of insufficiency fractures due to neoplasm or osteoporosis, and the timeframe of conservative treatment before additional intervention is considered.

2. In the study of devices for the treatment of insufficiency fractures due to neoplasm or osteoporosis, either for stabilization or reduction of the fracture, please discuss appropriate control groups and describe appropriate timeframes for comparison of

safety outcomes and effectiveness outcomes. Based upon your recommendations regarding appropriate control groups and timeframes for safety and effectiveness comparisons, when would be appropriate for control treatment to continue before allowing patients to crossover to the treatment group?

3. Many of the devices used in vertebroplasty (e.g., high and low modulus bone cements and other non-resorbable and absorbable bone cement alternatives) are polymerized in situ and have either toxic monomers, copolymers, accelerators, or initiators. In addition to the adverse events known to occur with devices used in vertebroplasty, the FDA currently asks sponsors to collect additional information on specific aspects of safety including infection, neurological status and radiographic endpoints evaluating extravasations, adjacent fractures, osteolysis, fracture through the material at the level of repair, adjacent arthritis, secondary interventions, progression of disease and fusion at the level of treatment.

    ?? What animal study or clinical study time point(s) should be considered in evaluation of chemical and toxic effects of the device for short and long term implantation of the device?

    ?? Please discuss any additional safety assessments you feel are valuable for evaluating these implants,

4. The FDA currently asks that spine studies collect information on specific aspects of effectiveness using such tools as the pain scales, function/disability questionnaires (NDI and Oswestry), maintenance of neurological status, maintenance of vertebral height, and a quality of Life (SF-36, WOMAC) questionnaire.
5.
    ?? Please discuss what clinically relevant endpoints in clinical practice should be measured to prove efficacy for these types of products.
    ?? Please discuss the distribution of expected improvement in these evaluations
    ?? Please discuss at what point you would expect maximum level of improvement to occur using each of these assessment tools.
    ?? Please discuss any additional effectiveness assessments you feel are valuable for these implants,
    ?? Please discuss what degree of improvements would be expected as clinically significant for the successful use of these devices.